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Case report

Lethal methemoglobinemia and automobile exhaust inhalation

Merete Vevelstad [a], Inge Morild [b,*]

[a] Division of Forensic Toxicology and Drug Abuse, Norwegian Institute of Public Health (NIPH), P.O. Box 4404 Nydalen, N-0403 Oslo, Norway
[b] Section of Pathology, The Gade Institute, University of Bergen and Haukeland University Hospital, N-5021 Bergen, Norway

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ABSTRACT

Inhalation of automobile exhaust gas often leads to death by CO intoxication. In some cases the measured carbon monoxide hemoglobin saturation level (COHb) is considerably below what is considered to be lethal. The death in such cases has been attributed to a combination of a high CO_2 and a low O_2 tension. In a recent case the deceased was found dead in a car equipped with a catalytic converter, with a hose leading exhaust from the engine to the interior of the car. Analysis revealed a moderately elevated COHb and a high methemoglobin saturation level (MetHb) in peripheral blood. No ethanol, narcotics or drugs were detected.

Reports mentioning MetHb or methemoglobinemia in post-mortem cases are surprisingly scarce, and very few have related exhaust gas deaths to methemoglobinemia. High-degree methemoglobinemia causes serious tissue hypoxia leading to unconsciousness, arrhythmia and death. The existing literature in this field and the knowledge that exhaust fumes contain nitrogen oxide gases (NOx) that by inhalation and absorption can result in severe methemoglobinemia, led us to postulate that this death could possibly be attributed to a combination of methemoglobinemia and a moderately high COHb concentration.

1. Introduction

Carbon monoxide (CO) intoxication is common in accidents like house fire and leakage from the exhaust of engines, or from burning of organic material in confined spaces. Suicide committed by CO intoxication, by leading automobile exhaust gas into the interior of a vehicle, is a relatively common method of suicide. A carbon monoxide hemoglobin (COHb) saturation level of about 50% is generally considered as lethal, while 20–50% might be severely toxic [1]. During the last decades the introduction of catalytic converters in new cars has drastically reduced the amount of CO in the exhaust [2]. In some cases of suspected suicidal CO intoxications, COHb saturation levels below severely toxic or lethal levels are found. Although MetHb levels are usually not reported and the condition not mentioned, the cause of death in such cases has been attributed to a combination of a high CO_2 tension and a low O_2 tension. The following case report led us to question whether another mechanism could possibly be of importance in such deaths.

2. Case report

A 28-year-old man was found dead in an automobile, after having been missing from his home for many hours. He left home at 07.30 a.m. and was found 11.30 p.m. the same day. The car, a 1989 model Mercedes Benz 300 with a petrol (gasoline) engine, was equipped with a catalytic converter. It was driven more than 300,000 km. The car was found inside an old railway tunnel, parked 400 m from the opening of the tunnel. The left front door (driver's door) and the two rear doors were open when the police arrived, but the doors were probably opened by the deceased's brother, who found him. The deceased was lying between front and rear seats with his head leaning against the front passenger door. Lividity and rigor were consistent with this position. A garden hose was taped to the exhaust pipe, and the hose was emptying into the cab of the car. The motor of the car was not running, but the ignition was in "on" position, the car's fan was still running and the hood of the car was still warm. No alcohol or drugs were found in the car.

The deceased had probably been in the car for several hours after his death, which happened on a winter Friday with outside temperatures ranging from 7 to 11 °C. From the scene, the body was transported to a refrigerated room in this rural district (arrival 2 h after he was found) where it was kept for 48 h, during the weekend. After a 1.5 h transport by car to the university hospital the following Monday morning, the body was placed in another

* Corresponding author. Tel.: +47 5597 2560; fax: +47 5597 5139.
E-mail addresses: inge.morild@gades.uib.no, inge.morild@helse-bergen.no (I. Morild).

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refrigerated room until the autopsy 72 h later. The temperature in the refrigerated rooms was 4–6 °C. The autopsy on Thursday 5.5 days after the death revealed moderate autolytic changes with some slipping of the skin. Some pressure marks were found, consistent with the deceased's position in the car. No injuries were found and there were no macroscopic or microscopic signs of disease. Due to the circumstances, a preliminary diagnosis of CO intoxication was given, and the manner of death was registered as suicide.

3. Materials and methods

Post-mortem specimens of femoral venous blood and urine were collected during autopsy of the deceased at the Gade Institute, Haukeland University Hospital. The samples were collected in heparinised tubes containing 1% potassium fluoride as preservative, and sent by ordinary mail (at temperature above freezing) the same day for analysis at the laboratory in the Division of forensic toxicology and Drug Abuse, NIPH. Samples were received in the laboratory on Monday 3.5 days later (and about 9.5 days after death). An aliquot was drawn few hours after arrival, and was kept refrigerated until the weekly performed screening analysis for COHb and MetHb 8 days later (17.5 days after death). The blood sample was not frozen before analysis. Two weeks after analysis, the blood and urine samples were gradually frozen by a two-step procedure, and kept frozen at −20 °C until MetHb was re-analyzed 6 months later.

The blood sample was routinely screened for common drugs of abuse (cut-off values 54, 10, 87 and 85 ng/ml for amphetamines, cannabis, cocaine and opiates, respectively) using an immunological method (Enzyme Multiplied Immunossay Technique, EMIT II), for alcohols and acetone using head-space gas chromatography (HS-GC-FID), and for 63 drugs/metabolites using liquid chromatography–mass spectrometry (LC/MS-EI mode, described by Hoiseth et al. [3]). Urine was screened for common drugs of abuse using EMIT (amphetamines with cut-off value 0.30 μg/ml, cannabis 20 ng/ml, cocaine 0.30 μg/ml, opiates 0.30 μg/ml, benzodiazepines 0.20 μg/ml, methadone 0.30 μg/ml and buprenorphine 5 ng/ml), and for alcohols and acetone by HS-GC-FID.

Screening analysis of COHb and MetHb in post-mortem blood was performed by spectrophotometry with the automated instrument IL 682 CO-Oximeter from ILS Norway, according to the manufacturer's specifications [4]. The method uses anticoagulated hemolyzed blood, and is based on the fact that free and bound hemoglobin absorb light at different wavelengths, and that different hemoglobin species have different absorption spectra. As post-mortem blood is often non-homogeneous and thus unsuitable for oximetry, our samples are diluted by adding 2 ml Milli-Q water (ultrapure water) to 0.5 ml blood, and centrifuged for 5 min. 65 μl of the supernatant is aspirated into the instrument, a hemolyzing diluent is added (Triton), the sample is transferred to the cuvette, and monochromatic light at six specific wavelengths is passed through the cuvette: 535.0, 585.2, 594.5, 626.6, 638.3 and 667.8 nm. A photo-detector measures light intensity at the other side, and the output is used to generate absorbances. A computer calculates the fractional concentrations of the various Hb species present in the sample, and relative percentages of oxyHb, deoxyHb, COHb and MetHb as well as total Hb are determined. The operator reports that the accuracy of measurements is within ±1% for the each species when MetHb is below 10%. Our COHb results are linear in the 2–100% range, with RSD ±10% (CV) and accuracy 5%, and a COHb cut-off of 5% is used.

Our method is not validated for MetHb, as we use this spectrophotometric method for semi-quantitative screening analysis of COHb in relation to cause of death. The MetHb result, a byproduct of the COHb-screening, has, so far, in our laboratory been regarded as informative only because of MetHb's ability to interfere with COHb screening analysis. MetHb levels above 10% are known to result in a background spectrum which can lead to falsely reduced or negative readings for COHb. Consequently, when MetHb is detected above 30%, we perform a COHb confirmatory analysis with a specific and quantitative method, even when COHb screening is negative. For confirmatory CO analysis we use head-space gas chromatography (HS-GC) with capillary column separation, combined with atomic absorption spectrophotometry (AAS) for measurement of total iron. Potassium hexacyanoferrat is added to the sample to liberate CO from Hb, and CO is reduced to methane (CH_4) through the action of a catalyst at 380 °C, with detection of CH_4 by FID (Flame Ionization Detection). These methods are not validated (or used) for quantitative analysis of MetHb.

Publications about specific chromatographic methods for MetHb seem scarce, and we could not find any Norwegian laboratories performing such analyses. However, the great majority of scientific publications mentioning post-mortem MetHb results seem to have used spectrophotometric methods comparable to our method. The MetHb absorbance is reported to be directly related to the concentration of methemoglobin in the sample [5].

4. Results

In femoral venous blood a COHb saturation level of 18% was found, by quantitative analysis by HS-GC/atomic absorption spectrophotometry. No drugs, narcotics, alcohols or acetone were detected. In urine the only finding was an ethanol concentration of 0.03%. No putrefaction substances were observed in blood during head-space gas chromatography of alcohols, while traces were observed in the urine (n-propanol).

During the spectrophotometric screening analysis of COHb and MetHb in blood, an unusually high MetHb saturation level of 56.3% was found. OxyHb, deoxyHb and COHb were 12.2, 30.9 and 0.6%, respectively, and the sum was 100.0%. Total hemoglobin was 13.8 g/l. Repeated spectrophotometric analysis 6 months later, after long-term freezing, showed exactly the same MetHb result, while a doubled deoxyHb, slightly increased COHb and negative value for OxyHb was indicated.

5. Discussion

The tentative cause of death in this case was CO intoxication, by suicidal inhalation of automobile exhaust gas inside a car. The COHb level of 18% detected in peripheral blood was however only moderately elevated, and could not explain his death. There were no other toxicological findings of interest in the samples, except an unusually high MetHb level in blood. Based on the existing literature we believe that the cause of death in this case is hypoxia that could be due to methemoglobinemia in combination with a moderately elevated COHb level.

5.1. Carbon monoxide (CO) and catalytic converters

The circumstances indicate CO poisoning when a person is found dead in a car and the exhaust is led into the car by a hose. Closed environment exposure to automobile exhaust gas is well known to result in death within 30 min. Old gasoline engines may produce exhaust with up to 7% CO, and the exhaust will saturate the interior of a small garage in 15–30 min with a lethal concentration of CO [6].

The far below lethal COHb level in our case is, however, in accordance with the fact that the actual 1989-model car was originally equipped with a catalytic converter. Installation of catalytic converters in automobiles has reduced the likelihood of death resulting from the inhalation of exhaust fumes in confined spaces [7–10]. The catalytic conversion process removes CO, hydrocarbons and nitrogen oxide, and three-way catalytic converters are reported to eliminate >99% of CO emissions [11]. After driving more than 300,000 km, the capacity of the converter in our case may have been somewhat reduced, consistent with the detected COHb level.

There have been some reports in the literature of deaths where circumstances indicated CO poisoning, but where COHb levels were less than the 5% level reported in living smokers and city inhabitants [12–14]. These deaths have been attributed to O_2 depletion and CO_2 narcosis, which may very well be the case.

5.2. Methemoglobinemia

There is, however, a striking shortage of publications mentioning methemoglobinemia as a possible cause of death in such cases, and MetHb levels are seldom reported. In the cadaver blood of victims who survived a given period after a fire, high MetHb values (up to 37%) were found. These are reported to be caused by the inhalation of nitrogen oxides produced by burning plastic [15]. Regarding automobile exhaust gas cases, only three reports have related such cases to methemoglobinemia, all representing survivors [16–18]. Kumagai stated that in cases with cyanosis by vehicle exhaust, one should expect methemoglobinemia to exist simultaneously with CO-hemoglobinemia.

Methemoglobinemia is a rare but well known condition that can be congenital or acquired, and that can be life-threatening